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Dockets Management Branch (HFA-305)  
Food and Drug Administration  
12420 Parklawn Drive  
Room 1-23  
Rockville, Maryland 20857

**RE: Draft CPG on Commercialization of In Vitro Diagnostic Devices Labeled  
for Research Use Only or Investigational Use Only**

Dear Sir or Madam:

We understand that the Food and Drug Administration (FDA) is in the process of finalizing the draft compliance policy guide (CPG) referenced above. We are writing to remind FDA to observe the First Amendment limits on government regulation of commercial speech that have been reinforced in recent judicial decisions, before issuing a final CPG. Three federal courts, including the Circuit Court of Appeals for the District of Columbia, recently held various FDA policies restricting the abilities of companies to disseminate information or promote their products to be unconstitutional. In light of these opinions, FDA should carefully consider whether the policies expressed in its CPG are consistent with the constitutional boundaries delineated by the courts, bearing in mind that guidance documents that restrict free speech – even draft ones – are not immune from judicial review. See Washington Legal Foundation v. Kessler, 880 F. Supp. 26, 32-36 (D.D.C. 1995).

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### Draft IVD Compliance Policy Guide

The draft CPG proposes to limit the manner in which manufacturers may label and promote their in vitro diagnostic products labeled “For Research Use Only” or “For Investigational Use Only.” For example, the draft CPG says that “manufacturers, importers, and distributors of uncleared and approved IVD’s must remove any labeling statements that indicate that performance characteristics (e.g., sensitivity or specificity) or safety and effectiveness have been established for any indicated use.” Draft Compliance Policy Guide for FDA and Industry, Commercialization of In Vitro Diagnostic Devices (IVD’s) Labeled for Research Use Only or Investigational Use Only (Jan. 5, 1998) (“Guidance”), at 6. This limit applies even if the information is truthful and not misleading. See id. at 11. Promotional materials for analyte specific reagents may not “make any statement regarding analytical or clinical performance,” even if truthful and not misleading. Id. at 14.

Three recent judicial opinions holding FDA policies limiting speech to be overreaching from a constitutional perspective have emphasized that truthful and nonmisleading speech is protected by the First Amendment. The opinions show a reluctance by the courts to allow FDA to ban information that is truthful and nonmisleading. FDA should therefore evaluate the speech policies in the final IVD guidance to assure that it conforms to the contours of these decisions and the First Amendment.

### Washington Legal Foundation

At issue in the WLF case were two sets of guidance documents. One addressed the promotion of off-label uses by manufacturers who sponsored continuing medical education (“CME”) seminars. See Guidance for Industry, Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64074 (Dec. 3, 1997) (“CME Guidance”). This guidance established twelve factors for determining when the content of a scientific or educational program might be inappropriately influenced by the sponsor of a program, and therefore subject to regulation by the agency. The guidance also provided for an optional written agreement between the provider and the sponsor of a program, the purpose of which was to demonstrate that the sponsor did not inappropriately influence the content of a seminar.

The other guidances at issue in WLF involved the distribution of “enduring materials,” defined as reference texts and article reprints from medical and scientific journals. See 61 Fed. Reg. 52800 (Oct. 8, 1996). FDA permitted the dissemination of

journal articles that discussed FDA-approved products, provided that numerous restrictions were met. The dissemination of medical textbooks and compendia by manufacturers to health care professionals was subject to even more stringent restrictions.

The WLF court concluded that the restrictions in these guidances failed to meet the four-part test governing the constitutionality of limits on commercial speech established in Central Hudson Gas and Electric Corp. v. Public Serv. Comm'n of New York, 447 U.S. 557 (1980). Central Hudson held that restrictions on commercial speech are constitutionally permissible if 1) the speech at issue does not concern unlawful activity and is not inherently misleading, 2) the government has a substantial interest in controlling the speech, 3) the restrictions imposed on the speech advance the government's interest in a direct and material way, and 4) the government's chosen means are a reasonable match for the ends it seeks. Although the WLF court did find that FDA had identified a legitimate objective, it also found that the policies were "considerably more extensive than necessary to further the substantial government interest in encouraging manufacturers to get new uses on-label," WLF, 13 F. Supp. 2d at 73, and thus held that the fourth prong of the test was not met.

As a threshold matter, FDA argued that all claims that had not been approved by the agency were presumptively false. The court flatly disagreed:

In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are presumptively untruthful or misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe. . . . [T]he conclusions reached by a laboratory, scientist or university academic and presented in a peer-reviewed journal or text book, or the findings presented by a physician at a CME seminar are not 'untruthful' or 'inherently misleading' merely because the FDA has not yet had the opportunity to evaluate the claim.

Id. at 67.

FDA had specified two principal concerns to justify its policies: 1) ensuring that physicians receive accurate and unbiased information to enable them to make informed prescription choices, and 2) encouraging manufacturers to submit applications to FDA for approval of new uses and indications. The court disagreed with FDA that the first asserted governmental interest was legitimate:

In light of the fact that the Supreme Court has repeatedly rejected governmental attempts to equate less information with better decision-making, and in light of the fact that the FDA does not question a physician's evaluative skills when the

information comes from a source other than a drug manufacturer, concerns about a physician's ability to critically evaluate materials presented to him is not a 'substantial interest.'

Id. at 70.

Although the court said that the government's other asserted interest was a "substantial interest," it nevertheless found the restrictions imposed by FDA to unduly restrict speech, due to the availability of a less burdensome alternative to FDA's policies on off-label promotional activities – namely, the "full, complete, and unambiguous disclosure by the manufacturer" of its interests in the product(s) at issue. "Full disclosure not only addresses all of the concerns advanced by the FDA, but addresses them more effectively." Id. at 73. The court noted that full disclosure would make clear to physicians that a particular use of a product was unapproved by FDA, and physicians would thus be able to evaluate the message accordingly.

The court's finding that the speech policies were unconstitutional led to issuance of an injunction expressly barring FDA from prohibiting or restricting any pharmaceutical or medical device manufacturer or other person

- a) from disseminating or redistributing to physicians or other medical professionals any article concerning prescription drugs or medical devices previously published in a bona fide peer-reviewed professional journal, regardless of whether such article includes a significant or exclusive focus on uses of drugs or medical devices other than those approved by FDA and regardless of whether such article reports the original study on which FDA approval of the drug or device in question was based;
- b) from disseminating or redistributing to physicians or other medical professionals any reference textbook (including any medical textbook or compendium) or any portion thereof published by a bona fide independent publisher and otherwise generally available for sale in bookstores or other distribution channels where similar books are normally available, regardless of whether such reference textbook or portion thereof includes a significant or exclusive focus on uses of drugs or medical devices other than those approved by FDA; or
- c) from suggesting content or speakers to an independent program provider in connection with a continuing medical education seminar program or other symposium, regardless of whether uses of drugs and medical devices other than those approved by FDA are to be discussed.

Order Granting Summary Judgment and Permanent Injunction, C.A. No. 1:94CV01306 (RCL) (D.D.C. July 30, 1998), at 2-3 (emphasis added).

FDA subsequently filed a motion requesting the court to clarify, among other things, that the scope of the injunction is confined only to the guidance documents and does not apply to other laws, regulations, or policies of the agency concerning promotional activities, such as the Food and Drug Administration Modernization Act of 1997 (FDAMA) provisions. See Defendants' Motion to Alter or Amend the Judgment and For a Stay, C.A. No. 94-1306 (RCL) (D.D.C. Aug. 18, 1998).

On February 16, 1999, the court issued a memorandum opinion in which it ruled that its earlier injunction was intended to apply to the policies expressed in the guidance documents, and not just the guidance documents themselves. "[T]he Court found that the FDA's policies imposed an unconstitutional burden upon the plaintiff's First Amendment rights. Consequently, the Court will not amend the July 30, 1998 order and permanent injunction to limit it to the three Guidance Documents. Such limitation was never the Court's intention." WLF, slip op. at 7 (emphasis in original). Thus, the court clarified that the injunction applied to FDA's policies, not just the guidance documents.

Since the initial ruling in WLF, two other federal courts have had the opportunity to consider FDA policies governing the promotional activities of manufacturers. In both cases, the court held FDA's policies to be inconsistent with the Central Hudson test.

Western States Med. Ctr. Pharmacy v. Shalala, CV-S-98-01650-JBR (RLH) (D. Nev. Dec. 18, 1998) (slip op.), involved a challenge by pharmacies to two FDAMA provisions. One of these provisions permitted a pharmacy to compound drugs, provided that the pharmacy "does not advertise or promote the compounding of any particular drug, class of drug, or type of drug." 21 U.S.C. § 353a(c). In deciding whether a temporary restraining order (TRO) prohibiting the enforcement of this provision was warranted, the court analyzed the provision under the Central Hudson test for commercial speech. Although the court found that the government's asserted interest was a substantial one, it determined that the restriction was unconstitutional since the government failed to prove that its restriction on advertising directly advanced this governmental interest, and that the restriction was not more extensive than necessary to serve that interest. Because of a lack of evidence indicating that the third and fourth prongs of the Central Hudson test were satisfied, the court found that "the Pharmacies have demonstrated probable success on the merits on their claim that 21 U.S.C. § 353A(c) infringes on their First Amendment right of freedom of speech. . . ." Western States, slip op. at 10. A TRO restraining FDA from enforcing the statutory provision was issued.

Similarly, in a recent opinion by the Court of Appeals for the District of Columbia Circuit, four FDA regulations prohibiting certain health claims by dietary supplement manufacturers were invalidated as being unconstitutional restraints on speech. See Pearson v. Shalala, No. 98-5043, 98-5084 (D.C. Cir. Jan. 15, 1999) (slip op.). To make a health claim under the Dietary Supplement Health and Education Act of 1994 (DSHEA), a dietary supplement manufacturer must obtain pre-authorization of the claim from FDA. The plaintiffs in this case had applied to the agency for authorization of four health claims linking the consumption of certain supplements to the reduction in risk of certain diseases. The standard for authorization provides that a claim may be authorized when FDA determines,

based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

21 C.F.R. § 101.14(c).

The court analyzed the agency's restrictions on health claims under the Central Hudson test. It found that FDA had asserted substantial government interests, but rejected the government's claims that the restrictions directly advanced, and constituted a reasonable fit with, these ends. Specifically, it was skeptical that the health claims regulatory scheme directly promoted consumer health:

Because it is not claimed that the product is harmful, the government's underlying – if unarticulated – premise must be that consumers have a limited amount of either attention or dollars that could be devoted to pursuing health through nutrition, and therefore products that are not indisputably health enhancing should be discouraged as threatening to crowd out more worthy expenditures. We are rather dubious that this simplistic view of human nature or market behavior is sound, but in any event, it surely cannot be said that this notion ... is a direct pursuit of consumer health; it would seem a rather indirect route, to say the least.

Id. at 12 (citations omitted) (emphasis in original).

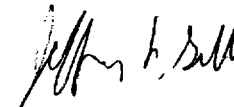
The Pearson court did say that “the existence of sufficient alternative channels of communication would count in [the government's] favor at the final step of Central Hudson.” Id. at 15 n.7 (citing Florida Bar v. Went for It, Inc., 515 U.S. 618 633-34 (1995)). The fact that dietary supplement manufacturers remained free to “publish articles and books concerning health claims” and “market ... dietary supplements with certain

physically separate peer-reviewed scientific literature,” however, did little to bolster the government’s position in the court’s view, since “those channels of communication reach consumers less effectively than does a claim made directly on the label because they impose higher search costs on consumers.” Id. (citations omitted). Thus, in essence, the court narrowly construed “sufficient alternatives” as consisting of only those that make information as readily available to the consumer as does a manufacturer’s label. The same analysis applies here to performance claims in the labeling of RUO and IUO in vitro products.

As a response to the government’s concern that consumers might assume that labels on dietary supplements are approved by the government, the court suggested a disclaimer in the nature of, “The FDA does not approve this claim.” Id. at 17. Similarly, the requirement of a prominent disclaimer stating any adverse effects would, in the court’s view, satisfy the governmental interest in ensuring the transmission of risk information to consumers. The court rejected the government’s claim that the disclaimers, in conjunction with the health claims, would confuse consumers, given that FDA offered no evidence, but only a “conclusory assertion” in support of this claim. In ultimately invalidating the four challenged regulations, the court made clear that “[a]lthough the government may have more leeway in choosing suppression over disclosure as a response to the problem of consumer confusion where the product affects health, it must still meet its burden of justifying a restriction on speech – here the FDA’s conclusory assertion falls far short.” Id. at 17-18 (citing Supreme Court cases discussing government’s burden).

FDA published the draft CPG without having the benefit of these three decisions. It is now clear that the Supreme Court’s commercial speech jurisprudence is being construed by the courts to favor the flow of more -- rather than less -- information regarding FDA-regulated products. In light of these recent precedents, we urge FDA to thoroughly evaluate its draft CPG on commercialization of RUO and IUO products, to ensure that the final document does not unconstitutionally limit the rights of manufacturers to provide truthful, nonmisleading information.

Sincerely,

A handwritten signature in black ink, appearing to read "Jeffrey N. Gibbs", written in a cursive style.

Jeffrey N. Gibbs

JNG/eam